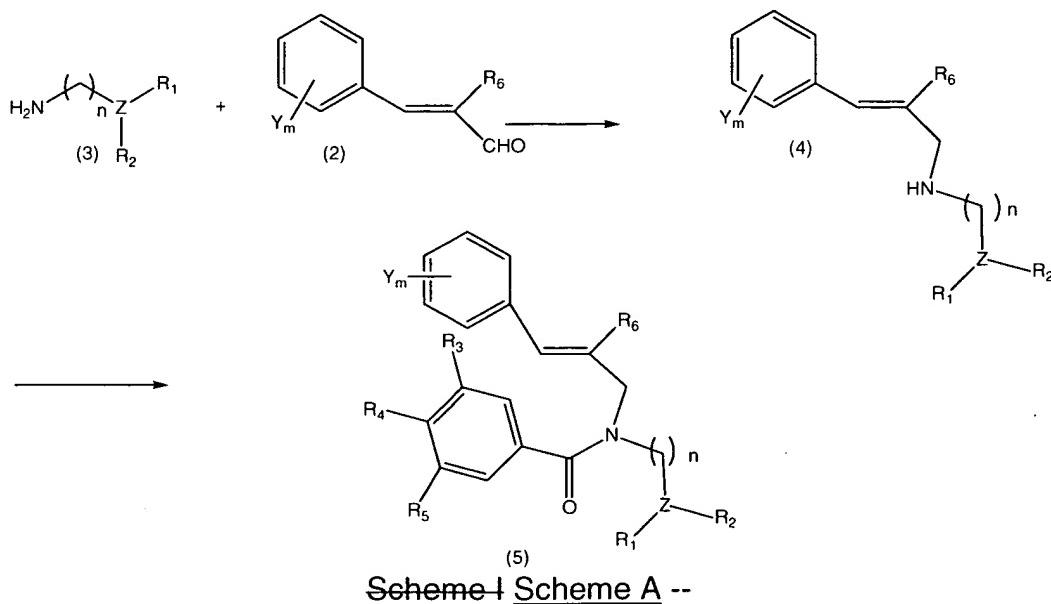


Amendments to the Specification

Please replace paragraph numbers [0013], [0065], [0067], [0075], [0078], [0089], [0090] and [00401] with the following corresponding paragraphs.

-- [0013] In another embodiment, compositions that include the modulators of the present invention and a pharmaceutically-acceptable carrier are disclosed. --

-- [0065] While many synthetic routes known to those of ordinary skill in the art may be used to synthesize the active compounds of the present invention, a general synthesis method is given below in Scheme I Scheme A.



-- [0067] The amination reaction may be carried out with a reducing agent in any suitable solvent, including, but not limited to tetrahydrofuran tetrahydrofuran (THF), dichloromethane, or methanol to form the intermediate (4). Suitable reducing agents for the condensation reaction include, but are not limited to, sodium cyanoborohydride (as described in Mattson, et al., J. Org. Chem. 1990,

55, 2552 and Barney, et al., Tetrahedron Lett. 1990, **31**, 5547); sodium triacethoxyborohydride (as described in Abdel-Magid, et al., Tetrahedron Lett. 1990, **31**, 5595); sodium borohydride (as described in Gribble; Nutatis Synthesis. 1987,709); iron pentacarbonyl and alcoholic KOH (as described in Watabane, et al., Tetrahedron Lett. 1974, 1879); and BH₃-pyridine (as described in Pelter, et al., J. Chem. Soc., Perkin Trans. 1, 1984, 717). --

-- [0075] Aqueous suspensions may also contain the active compositions in ~~admixture~~ a mixture with excipients suitable for the manufacture of aqueous suspensions. Such excipients are often referred to as suspending agents, dispersing agents, or wetting agents. Preferable suspending agents include, for example, sodium carboxymethylcellulose, methylcellulose, hydroxy-propylmethylcellulose, sodium alginate, polyvinyl- pyrrolidone, gum tragacanth, and gum acacia. --

-- [0078] Dispersible powders and granules suitable for preparation of an aqueous suspension by the addition of water provide the active ingredient in ~~admixture~~ a mixture with a dispersing or wetting agent, a suspending agent, and one or more preservatives. Suitable dispersing or wetting agents and suspending agents are exemplified by those already mentioned above. Additional excipients, for example sweetening, flavoring and coloring agents, may also be present. --

-- [0089] While not wishing to be bound by any particular theory, the compositions of the present invention are believed to provide a method of inhibiting the binding of SDF-1 and/or I-TAC to the CCXCKR2 receptor. SDF-1 is known to provide a target for interfering with the development or spread of cancer cells in a mammal, such as a human. As shown below in examples 24-26 paragraphs 406 - 408,

inhibition of the binding of I-TAC to the CCXCKR2 receptor prevents the formation of vascularized tumors. By contacting the compositions described above with a cancer cell that expresses the CCXCKR2 receptor, the invasive response that would otherwise trigger in the cancer cell can be reduced. Accordingly, the present invention is also directed to methods that are useful in the prevention and/or treatment of cancer, particularly solid tumor cancers, more particularly breast cancer. --

-- [0090] As determined by radiolabeled SDF-1 binding and I-TAC displacement, CCXCKR2 was preferentially expressed in human transformed cells. Included in ~~TABLE 2~~ TABLE 1 are those tissue types in which CCXCKR2 was expressed (CCXCKR2⁺) as well as those tissue types in which CCXCKR2 was not expressed (CCXCKR2⁻).

TABLE 2 TABLE 1 --

-- [00401] Compounds that were deemed effective modulators were able to displace at least 50% of either of the chemokines SDF-1 or I-TAC from the CCXCKR2 receptor at concentrations at or below 1.1 micromolar (μ M) and more preferably at concentrations at or below 300 nanomolar (nM). At present, especially preferred compounds can displace at least 50% of the SDF-1 or I-TAC from the CCXCKR2 receptor at concentrations at or below 200 nM. Exemplary compounds that met these criteria are reproduced in ~~Table 1~~ TABLE 2 below.

TABLE 1 TABLE 2 --

Please replace the following Example titles as shown. These titles appear before paragraph numbers [00194], [00197], [00200], [00252], [00284], [00288],

[00292], [00296], [00299], [00303], [00307], [00310], [00314], [00318], [00321] and [00398].

-- ~~Example 34~~ Example 35: N-(S)-(1-Cyclohexylmethyl-pyrrolidin2-yl-methyl)-3,4,5-trimethoxy-N-(2-methyl-3-phenyl-allyl)-benzamide --

-- ~~Example 35~~ Example 36: 3,4,5-Trimethoxy-N-(2-methyl-3-phenyl-allyl)-N-(R)-pyrrolidin-2-ylmethyl-benzamide --

-- ~~Example 36~~ Example 37: N-[3-(4-Fluoro-phenyl)-2-methyl-allyl]-3,4,5-trimethoxy-N-pyrrolidin-2-ylmethyl-benzamide --

-- ~~Example 57~~ Example 56: N-[1-(S)-(1-Cyclohexyl-ethyl)-pyrrolidin-2-ylmethyl]-N-[3-(2,4-difluoro-phenyl)-2-methyl-allyl]-3,4,5-trimethoxy-benzamide --

-- ~~Example 67~~ Example 66: 2,3-Dihydro-benzo[1,4]dioxane-6-carboxylic acid (S)-(1-cyclohexylmethyl-pyrrolidin-2-ylmethyl)-(2-methyl-3-phenyl-allyl)-amide --

-- ~~Example 68~~ Example 67: N-(S)-(1-Cyclohexylmethyl-pyrrolidin-2-ylmethyl)-3,4-dimethoxy-N-(2-methyl-3-phenyl-allyl)-benzamide --

-- ~~Example 69~~ Example 68: N-(S)-(1-Cyclohexylmethyl-pyrrolidin-2-ylmethyl)-3,4-diethoxy-N-(2-methyl-3-phenyl-allyl)-benzamide --

-- ~~Example 70~~ Example 69: N-(S)-(1-Cyclohexylmethyl-pyrrolidin-2-ylmethyl)-3,4-diisopropoxy-N- (2-methyl-3-phenyl-allyl)-benzamide --

-- Example 71 Example 70: 7-Methoxy-2,2-dimethyl-benzo[1,3]dioxole-5-carboxylic acid-(S)-(1-cyclohexylmethyl-pyrrolidin-2-ylmethyl)-(2-methyl-3-phenyl-allyl)-amide --

-- Example 72 Example 71: N-(S)-(1-Cyclohexylmethyl-pyrrolidin-2-ylmethyl)-3-difluoromethoxy-4-methoxy-N-(2-methyl-3-phenyl-allyl)-benzamide --

-- Example 73 Example 72: N-(S)-(1-Cyclohexylmethyl-pyrrolidin-2-ylmethyl)-4-difluoromethoxy-methoxy-N-(2-methyl-3-phenyl-allyl)-benzamide --

-- Example 74 Example 73: 7-Difluoromethoxy-2,2-dimethyl-benzo[1,3]dioxole-5-carboxylic acid (S)-(1-cyclohexylmethyl-pyrrolidin-2-ylmethyl)-(2-methyl-3-phenyl-allyl)-amide --

-- Example 75 Example 74: 2,2-Difluoro-benzo[1,3]dioxole-5-carboxylic acid (S)-(1-cyclohexyl-pyrrolidin-2-ylmethyl)-(2-methyl-3-phenyl-allyl)-amide --

-- Example 76 Example 75: N-(S)-(1-Cyclohexyl-pyrrolidin-2-ylmethyl)-3,4-dimethoxy-N-(2-methyl-3-phenyl-allyl)-benzamide --

-- Example 77 Example 76: 7-Methoxy-2,2-dimethyl-benzo[1,3]dioxole-5-carboxylic acid (S)-(1-cyclobutyl- pyrrolidin-2-ylmethyl)-(2-methyl-3-phenyl-allyl)-amide --

-- Example 102 Example 100: 3,4,5-Trimethoxy-N-(2-methyl-3-phenyl-allyl)-N-(2-piperidin-1-yl-ethyl)-benzamide --